Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the present application.

Listing of Claims

1. (currently amended) A method of treating a Pervasive Developmental Disorder selected from the group consisting of Asperger's Disorder, Rett's Disorder, Childhood Disintegrative Disorder, and Pervasive Developmental Disorder Not Otherwise Specified, comprising administering to a patient in need of such treatment an effective amount of a norepinephrine reuptake inhibitor selected from the group consisting of:

atomoxetine or a pharmaceutically acceptable salt thereof; and racemic reboxetine or a pharmaceutically acceptable salt thereof; (S,S) reboxetine or a pharmaceutically acceptable salt thereof; a compound of formula (I):

wherein X is C_1 - C_4 alkylthio, and Y is C_1 - C_2 alkyl, or a pharmaceutically acceptable salt thereof; as sole active agent.

a compound of formula (IA):

wherein n is 1, 2 or 3; R1 is C₂-C₁₀alkyl, C₂-C₁₀alkenyl, C₃-C₈eycloalkyl or C₄-C₁₀eycloalkylalkyl, wherein one C-C bond within any cycloalkyl moiety is optionally substituted by an O-C or C=C bond and wherein each group is optionally substituted with Page 2 of 10

from 1 to 7 halogen substituents and/or with from 1 to 3 substituents each independently selected from hydroxy, cyano, C1-C4alkyl and C1-C4alkoxy; R2 is H, C1-C4alkyl (optionally substituted with from 1 to 7 halogen atoms), C₁-C₄alkyl-S(O)_x-wherein x is 0, 1 or 2 (optionally substituted with from 1 to 7 halogen atoms), C₁-C₄alkoxy (optionally substituted with from 1 to 7 halogen atoms), cyano, halogen, phenyl (optionally substituted with from 1 to 3 substituents each independently selected from halogen, C1-C4alkyl and C1-C4alkoxy), phenoxy (optionally substituted with from 1 to 3 substituents each independently selected from halogen, C1-C4alkyl and C1-C4alkoxy) or CO2(C1-C4alkyl), or together with R3 forms a further benzene ring (optionally substituted with from 1 to 3 substituents each independently selected from halogen, C1-C4alkyl and C1-C4alkoxy); R3 is H, C1-C4alkyl (optionally substituted with from 1 to 7 halogen atoms), C₁-C₄alkyl-S(O)_x-wherein x is 0, 1 or 2 (optionally substituted with from 1 to 7 halogen atoms), C1-C4alkoxy (optionally substituted with from 1 to 7 halogen atoms), cyano, halogen, phenyl (optionally substituted with from 1 to 3 substituents each independently selected from halogen, C1-C4alkyl and C1-C₄alkoxy), phenoxy (optionally substituted with from 1 to 3 substituents each independently selected from halogen, C1-C4alkyl and C1-C4alkoxy) or -CO2(C1-C4alkyl), or together with R2 or R4 forms a further benzene ring (optionally substituted with from 1 to 3 substituents each independently selected from halogen, C₁-C₄alkyl and C₁-C₄alkoxy); R4 is H, C₁-C₄alkyl (optionally substituted with from 1 to 7 halogen atoms), C₁-C₄alkyl-S(O)_x-wherein x is 0, 1 or 2 (optionally substituted with from 1 to 7 halogen atoms), C₁-C₄alkoxy (optionally substituted with from 1 to 7 halogen atoms), evano, halogen, phenyl (optionally substituted with from 1 to 3 substituents each independently selected from halogen, C1-C4alkyl and C1-C4alkoxy), phenoxy (optionally substituted with from 1 to 3 substituents each independently selected from halogen, C1-C4alkyl and C1-C4alkoxy) or -CO2(C1-C₄alkyl), or together with R3 forms a further benzene ring (optionally substituted with from 1 to 3 substituents each independently selected from halogen, C₁-C₄alkyl and C₁-C₄alkoxy); R5 is H, C1-C4alkyl (optionally substituted with from 1 to 7 halogen atoms), C1-C4alkoxy (optionally substituted with from 1 to 7 halogen atoms) or halogen; R6 is H, C1-C4alkyl (optionally substituted with from 1 to 7 halogen atoms), C1-C1alkoxy (optionally substituted with from 1 to 7 halogen atoms) or halogen; R7 is H or C1-C4alkyl; R8 is H or C1-C4alkyl; R9 is H, halogen, hydroxy, cyano, C1-C4alkyl or C1-C4alkoxy; and R10 is H, halogen, hydroxy, cyano, C₁-C₄alkyl or C₁-C₄alkoxy; or a pharmaceutically acceptable salt thereof, with the proviso that the compound N ethyl-N benzyl 4 piperidinamine is excluded;

a compound of formula (IB):

wherein Rx is H; Ry is H or C_1 - C_4 alkyl; each Rz is independently H or C_1 - C_4 -alkyl; X represents O; Y represents OH or OR; R is C_1 - C_4 -alkyl; Ar_1 is a phenyl ring or a 5- or 6-membered heteroaryl ring each of which may be substituted with 1, 2, 3, 4 or 5 substituents (depending upon the number of available substitution positions) each independently selected from C_1 - C_4 -alkyl, $O(C_1$ - C_4 -alkyl), $S(C_1$ - C_4 -alkyl), halo, hydroxy, pyridyl, thiophenyl and phenyl optionally substituted with 1, 2, 3, 4 or 5 substituents each independently selected from halo, C_1 - C_4 -alkyl, or $O(C_1$ - C_4 -alkyl); and Ar_2 -is a phenyl ring or a 5- or 6 membered heteroaryl ring each of which may be substituted with 1, 2, 3, 4 or 5 substituents (depending upon the number of available substitution positions) each independently selected from C_1 - C_4 -alkyl, $O(C_1$ - C_4 -alkyl) and halo; wherein each above mentioned C_1 - C_4 -alkyl group is optionally substituted with one or more halo atoms; or a pharmaceutically acceptable salt thereof;

a compound of formula (IC)

$$\begin{array}{c|c}
R^1 & A \\
\hline
R^1 & X \\
\hline
R^1 & R^1 \\
\hline
(IC)$$

wherein: A is S or O; R is H; Ar is a phenyl group optionally substituted with 1, 2, 3, 4 or 5 substituents each independently selected from C₁-C₄-alkyl, O(C₁-C₄-alkyl), S(C₁-C₄ alkyl), halo, hydroxy, CO₂(C₁-C₄-alkyl), pyridyl, thiophenyl and phenyl optionally substituted with 1, 2, 3, 4 or 5 substituents each independently selected from halo, C₁-C₄ alkyl, or O(C₁-C₄-alkyl); X is a phenyl group optionally substituted with 1, 2, 3, 4 or 5 substituents each independently selected from halo, C₁-C₄-alkyl, or O(C₁-C₄-alkyl); a C₁-C₄ Page 4 of 10

alkyl group; a C₃-C₆ cycloalkyl group or a CH₂(C₃-C₆ cycloalkyl) group; R' is H or C₁-C₄ alkyl; each R¹-is independently H or C₁-C₄ alkyl; wherein each above mentioned C₁-C₄ alkyl group is optionally substituted with one or more halo atoms; or a pharmaceutically acceptable salt thereof; with the proviso that, when A is O, X is a C₁-C₄ alkyl group, a C₃-C₆ cycloalkyl group or a CH₂(C₃-C₆ cycloalkyl) group;

a compound of formula (ID)

$$\begin{array}{c|c} & & & \\ & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\$$

(ID)

wherein -X- is $-C(R^4R^5)$, O- or S-; n is 2 or 3; R^1 is H or C_1 - C_4 alkyl; R^3 is H, halo, C_1 - C_4 alkyl, $O(C_1$ - C_4 alkyl), nitrile, phenyl or substituted phenyl; R^4 and R^5 are each independently selected from H or C_1 - C_4 alkyl; Ar- is selected from the group consisting of

(i)
$$R^{2a}$$
 and (ii) R^{2e} R^{2d}

in which R^{2a} is H, halo, methyl or ethyl; R^{2b} is H, halo or methyl; R^{2e} is H, halo, methyl, trifluoromethyl, nitrile, or methoxy; R^{2d} is H, halo, methyl or ethyl; R^{2e} is H, halo, methyl, trifluoromethyl, nitrile, or methoxy; R^{2f} is H, or fluoro; Y is O, S or $N(R^6)$; and R^6 is H or methyl or a pharmaceutically acceptable salt thereof;

a compound of formula (IE)

$$\begin{array}{c|c}
R^2 & R^1 \\
\hline
 & N \\
 & R^3 & R^4
\end{array}$$

(IE)

wherein R^4 is C_1 - C_6 alkyl (optionally substituted with 1, 2 or 3 halo substituents and/or with 1 substituent selected from -S-(C_1 - C_3 alkyl), -O-(C_1 - C_3 alkyl) (optionally substituted with 1, 2

or 3 F atoms), O (C_3 C_6 cycloalkyl), SO_2 (C_4 C_3 alkyl), CN, COO (C_4 C_2 alkyl) and OH); C_2 C_6 alkenyl; $(CH_2)_q$ Ar_2 ; or a group of formula (i) or (ii)

$$(CH_2)_r Z$$

$$(CR^5R^6)_s (CR^7R^8)_{t-X} (CR$$

R², R³ and R⁴ are each independently selected from hydrogen or C₁-C₂ alkyl; R⁵, R⁶, R⁷ and R⁸ are at each occurrence independently selected from hydrogen or C₁-C₂ alkyl; -X-is a bond, -CH₂-, -CH=CH-, -O-, -S-, or -SO₂-; -Y- is a bond, -CH₂- or -O-; -Z is hydrogen, -OH or $O(C_1 - C_2)$ alkyl); p is 0, 1 or 2; q is 0, 1 or 2; r is 0 or 1; s is 0, 1, 2 or 3; t is 0, 1, 2 or 3; Ar₁ is phenyl, pyridyl, thiazolyl, benzothiophenyl or naphthyl; wherein said phenyl, pyridyl or thiazelyl group may be substituted with 1, 2 or 3 substituents each independently selected from halo, cyano, C₁-C₄-alkyl (optionally substituted with 1, 2 or 3 F atoms), O (C₁-C₄ alkyl) (optionally substituted with 1, 2 or 3 F atoms) and -S-(C₁-C₄-alkyl) (optionally substituted with 1, 2 or 3 F atoms) and/or with 1 substituent selected from pyridyl, pyrazole, phenyl (optionally substituted with 1, 2 or 3 halo substituents) and phenoxy (optionally substituted with 1, 2 or 3 halo substituents); and wherein said benzothiophenyl or naphthyl group may be optionally substituted with 1, 2 or 3 substituents each independently selected from halo, eyano, C₁-C₄-alkyl (optionally substituted with 1, 2 or 3 F atoms), O-(C₁-C₄ alkyl) (optionally substituted with 1, 2 or 3 F atoms), and S (C₁-C₄ alkyl) (optionally substituted with 1, 2 or 3 F atoms); Ar₂ is naphthyl, pyridyl, thiazolyl, furyl, thiophenyl, benzothiophenyl, or phenyl, wherein said naphthyl, pyridyl, thiazolyl, furyl, thiophenyl, benzothiophenyl, or phenyl may be substituted with 1, 2 or 3 substituents each independently selected from halo, C₁-C₄ alkyl (optionally substituted with 1, 2 or 3 F atoms) and O (C₁-C₄ alkyl) (optionally substituted with 1, 2 or 3 F atoms); or a pharmaceutically acceptable salt thereof; provided that (a) the cyclic portion of the group of formula (i) must contain at least three carbon atoms and not more than seven ring atoms; (b) when X is CH-CH, then the cyclic portion of the group of formula (i) must contain at least five carbon atoms; and (c) when Z is OH or O-(C₁-C₂-alkyl), then X- is -CH₂-; (d) when Y- is O- then p cannot be 0; and (e) the compound 3-[(phenylmethyl) (3S) 3-pyrrolidinylamino] propanenitrile is excluded;

a compound of formula (IF)

$$\begin{array}{c|c}
R^2 & R^1 \\
\hline
 & N & Ar_1 \\
\hline
 & R^3 & R^4
\end{array}$$
(IF)

wherein

is a group of formula (a) or (b)

$$R^2$$
 R^2
 R

R¹ is C₁-C₆ alkyl (optionally substituted with 1, 2 or 3 halo substituents and/or with 1 substituent selected from -S-(C₁-C₂-alkyl), -O-(C₁-C₃-alkyl) (optionally substituted with 1, 2 or 3 F atoms), -O-(C₃-C₆-cycloalkyl), -SO₂-(C₁-C₃ alkyl), -CN, -COO-(C₁-C₂-alkyl) and OH); C2-C6-alkenyl; -(CH2)q-Ar2; or a group of formula (i) or (ii)

$$(CH_2)_r$$
 Z $(CR^5R^6)_s$ $(CH_2)_r$ (CR^5R^6) $(CH_2)_p$ $(CR^7R^8)_t$ $(CR^7R^$

 R^2 , R^3 -and R^4 -are each independently selected from hydrogen or C_1 - C_2 alkyl; R^5 , R^6 , R^7 -and R8-are at each occurrence independently selected from hydrogen or C1-C2 alkyl; -X- is a bond, -CH₂-, CH=CH-, O , S , or SO₂-; -Y is a bond, -CH₂-or -O ; Z is hydrogen, OH or -O (C₁-C₃-alkyl); p is 0, 1 or 2; q is 0, 1 or 2; r is 0 or 1; s is 0, 1, 2 or 3; t is 0, 1, 2 or 3; Ar₁ is phenyl, pyridyl, thiazolyl, benzothiophenyl or naphthyl; wherein said phenyl, pyridyl or thiazolyl-group may be substituted with 1, 2 or 3 substituents each independently selected from halo, cyano, C₁-C₄ alkyl (optionally substituted with 1, 2 or 3 F atoms), O (C₁-C₄ alkyl) (optionally substituted with 1, 2 or 3 F atoms) and S (C₁ C₄ alkyl) (optionally substituted

with 1, 2 or 3 F atoms) and/or with 1 substituent selected from pyridyl, pyrazole, phenyl (optionally substituted with 1, 2 or 3 halo substituents); and wherein said benzothiophenyl or naphthyl group may be optionally substituted with 1, 2 or 3 substituents each independently selected from halo, eyano, C₁-C₄ alkyl (optionally substituted with 1, 2 or 3 F atoms), O (C₁-C₄ alkyl) (optionally substituted with 1, 2 or 3 F atoms), and S (C₁-C₄ alkyl) (optionally substituted with 1, 2 or 3 F atoms); Ar₂ is naphthyl, pyridyl, thiazolyl, furyl, thiophenyl, benzothiophenyl, or phenyl, wherein said naphthyl, pyridyl, thiazolyl, furyl, thiophenyl, benzothiophenyl, or phenyl may be substituted with 1, 2 or 3 substituents each independently selected from halo, C₄-C₄ alkyl (optionally substituted with 1, 2 or 3 F atoms) and O (C₁-C₄ alkyl) (optionally substituted with 1, 2 or 3 F atoms) and O (C₁-C₄ alkyl) (optionally substituted with 1, 2 or 3 F atoms) and O (C₁-C₄ alkyl) (optionally substituted with 1, 2 or 3 F atoms) and O (C₁-C₄ alkyl) (optionally substituted with 1, 2 or 3 F atoms). The contain at least three carbon atoms and not more than seven ring atoms; (b) when X is CH=CH, then the cyclic portion of the group of formula (i) must contain at least five carbon atoms; and (c) when Z is OH or O (C₁-C₃ alkyl), then X is CH₂; and (d) when Y is O- then p cannot be 0; and

a compound of formula (IG)

wherein -X is -S or -O; each R is independently selected from H or C₁-C₄ alkyl; R¹ is H, C₁-C₄ alkyl, C₁-C₄ alkoxy, halo, cyano, trifluoromethyl, trifluoromethoxy, -NR³R⁴, -CONR³R⁴, -COOR³ or a group of the formula (i)

$$-z$$
 R^5

R²-is C₁-C₄-alkyl, phenyl or phenyl substituted with 1, 2 or 3 substituents each independently selected from C₁-C₄-alkyl, C₁-C₄-alkoxy, nitro, hydroxy, cyano, halo, trifluoromethyl,

International Serial No. PCT/US2004/025593 Docket No. X16410

trifluoromethoxy, benzyl, benzyloxy, $-NR^6R^7$, $-CONR^6R^7$, $-COOR^6$, $-SO_2NR^6R^7$ and $-SO_2R^6$; R^5 is selected from $-C_1$ - $-C_4$ alkyl, $-C_4$ -alkoxy, carboxy, nitro, hydroxy, eyano, halo, trifluoromethyl, trifluoromethoxy, benzyl, benzyloxy, $-NR^8R^9$, $-CONR^8R^9$, $-SO_2NR^8R^9$ -and $-SO_2R^8$; R^3 , R^4 , R^6 , R^7 , R^8 and R^9 are each independently selected from H or $-C_4$ -alkyl; and $-C_4$ -is a bond, $-C_4$ - $-C_4$ -alkyl; and

or a pharmaceutically acceptable salt thereof.

- 2. (cancelled)
- 3. (cancelled)
- 4. (currently amended) The method of claim 1 or 3, or the use of claim 2 or 3, wherein said selective norepinehprine reuptake inhibitor is atomoxetine hydrochloride.
- 5. (newly added) The method of claim 1, wherein attention-deficit/hyperactivity disorder occurs comorbidly with said Pervasive Developmental Disorder.
- 6. (newly added) The method of claim 4, wherein attention-deficit/hyperactivity disorder occurs comorbidly with said Pervasive Developmental Disorder.